IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In Re the Application of:	Group Art Unit: 1617
THOR	Examiner: Yong Soo Chong
Serial No.: 10/049,427	Confirmation No.: 1087
Filed: May 6, 2002	REPLY TO EXAMINER'S ANSWER PURSUANT TO 37 C.F.R. § 41.41
Atty. File No.: 4220-78-PUS	*Filed Electronically*
For: "Methods of Using Rapid-Onset Selective Serotonin Reuptake Inhibitors for Treating Sexual Dysfunction"	

Board of Patent Appeals and Interferences
Commissioner for Patents
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This Reply to Examiner's Answer is being filed in response to the Examiner's Answer dated August 10, 2007 ("Answer") pursuant to 37 CFR § 41.41 and is being timely filed within two months of the date of the Answer. Submitted herewith is a Request for Oral Hearing pursuant to 37 CFR § 41.47 accompanied by the fee set forth in 37 CFR § 41.20(b)(3).

Contention 1.1

The Answer addresses Appellant's Contention 1.1[1] at p. 5, l. 13-p. 6, l. 12 by noting that "[n]owhere in the reference [McMahon et al.], especially in Study 1, does it state the need to administer a priming dose or refer to a priming dose effect." The Answer appears to conclude that, since McMahon does not refer to a priming dose, the skilled person would rely on McMahon et al. as demonstrating that paroxetine is effective to treat PE in the absence of a priming dose. However, a skilled person would reach the opposite conclusion, namely, if the McMahon et al. investigation did not consider priming dose effects, no conclusions could be reached about whether

[1] Appellant's Contention 1.1 states "The Examiner has mistakenly construed the 'as-needed' use of paroxetine as described in McMahon et al. as demonstrating effectiveness to treat premature ejaculation 'as-needed in the absence of priming doses.'"

paroxetine is effective without a priming dose. This conclusion is fully supported by the Rivas Declaration in which Dr. Rivas, after review of McMahon et al., concludes that it does not provide sufficient information for the skilled person to determine that paroxetine is effective to treat premature ejaculation as-needed in the absence of priming doses. (Rivas Decl., ¶ 4.f.)

In response to the argument in the Rivas Declaration that the McMahon et al. study did not impose a minimum time interval between intercourse episodes and therefore, one dose of paroxetine may not have been cleared from the body at the time of a subsequent dose, the Answer asserts that "there is no doubt that paroxetine still increases mean ejaculatory latency without daily dosing." (Answer, p. 6, ll. 5-12) This statement confounds (1) the absence of a three week period of daily dosing before as-needed dosing (i.e., the protocol of McMahon et al.'s Study 1) with (2) a protocol that would ensure an absence of priming dose effects. The McMahon et al. study did not include the latter and therefore, no conclusion can be reached about efficacy of paroxetine in the absence of priming doses.

Contention 1.2

The Answer addresses Appellant's Contention 1.2[2] at p. 6, l. 13-p. 8, l. 4 by reiterating arguments from prosecution to the effect that the so-called "week 1 data" (e.g., data as shown in Fig. 1, week 1) are statistically significant (and therefore, can be relied upon as demonstrating efficacy of paroxetine in the absence in the absence of priming doses). As discussed in Contention 1.2 in Appellant's Brief, these arguments are contrary to McMahon et al.'s statement that the data for Groups A and B in Study 1 were statistically superior to placebo at 2, 3 and 4 weeks (clearly implying the week 1 data were not statistically superior) (McMahon et al., p. 1827, sentence bridging cols. 1-2), as well as Dr. Rivas' understanding of McMahon et al.'s statement. (Rivas Decl., ¶ 3.a.) In addition, Dr. Rivas' review of McMahon et al. led him to conclude that it does not provide sufficient information to determine whether the week 1 treatment data of Study 1 are statistically significantly different from the control data. (Rivas Decl., ¶ 3.b.)

As an alternative, the Answer appears to take the position that a data point that

is different from a baseline value can be relied upon as proving an effect without regard to whether the data point is ***statistically significantly different*** from the baseline. (Answer, p. 7, ll.18-21) This position is simply contrary to basic precepts of science.

Although the Answer does not challenge the definition of a priming dose (a prior dose of a drug that has not been cleared from the body at the time of administration of a subsequent dose of the drug (Rivas Decl., ¶ 5)), the Answer continues to misunderstand the term to mean the first administration of a drug, regardless of whether it is cleared from the body. (Answer, p. 7, ll. 5-8)

Contention 1.4

The Answer reiterates various arguments from early in prosecution regarding Lane and the Swartz reference discussed in Lane at p. 9, l. 12-p. 10, l. 22. However, the Answer does not rebut Contention 1.4 that Lane (and the Swartz abstract mentioned in Lane) does not disclose the as-needed use of SSRI's to treat premature ejaculation being effective in the absence of priming doses.

Contention 2

The Answer addresses Appellant's Contention 2[3] at p. 11, ll. 1-20 by stating that this Contention is not persuasive because of "new rationales" for an analysis of obviousness in the Supreme Court's decision in KSR International Co. v. Teleflex Inc., 127 S. Ct. 1727 (2007). As discussed below, while the KSR decision set out defined conditions in which a solution to a problem that is "obvious to try" is also "obvious" for purposes of 35 USC § 103, the presently claimed invention does not meet those defined conditions of "a finite number of identified, predictable solutions".

The Answer characterizes the "new rationales" as including "simple substitution of one known element for another to obtain predictable results and applying an 'obvious to try' rationale where one is choosing from a finite number of identified, predictable solutions, with a reasonable expectation of success." (Answer, p. 11, ll. 6-9). The Answer states that dapoxetine, as disclosed by Eli Lilly and Robertson, can be substituted for the SSRIs disclosed in McMahon et al. and Lane,

[2] Appellant's Contention 1.2 states "The Examiner is mistakenly relying on the week 1 data in McMahon et al. as being statistically significant and as showing effective treatment of premature ejaculation in the absence of priming doses."

and that Eli Lilly and Robertson disclose a finite number of SSRIs.

In the portion of the KSR decision referenced by the Answer, the Court states:

> When there is a design need or market pressure to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill in the art has good reason to pursue the known options within his or her technical grasp.

KSR Int'l Co., 127 S. Ct. at 1740.

By asserting that this analysis applies to the case, the Answer is supposing that there are first a "finite number" of potential solutions and that it is "predictable" how these solutions will work. While even very large numbers are "finite", in the context of the KSR decision, the term "finite number" should be understood to refer to a relatively small finite number since in the facts of the KSR decision, the court was analyzing the number of options for placement of an electronic control sensor to be placed in a vehicle control pedal apparatus having three other parts: a support, a pedal assembly and a pivot. Thus, in the context of the KSR analysis, a "finite number" referred to three options.

In the context of the present application and the cited references, the number of potential "solutions" (i.e., compounds for effectively treating premature ejaculation as needed in the absence of priming doses) is significantly larger than the "finite number" of options in the KSR decision and therefore, is distinguishable. As the Answer notes (p. 11, ll. 12), Lane teaches that SSRIs generally "may be of use in the management of premature ejaculation," (Lane, p. 79, col. 1, lines 24-25) and even more broadly than acknowledged by the Answer that "serotonergic drugs . . . have indicated potential efficacy in the management of premature ejaculation" (Lane, p. 79, col. 1, ll. 39-45). While McMahon et al. only evaluates paroxetine, it generally references in the background section relied upon by the rejection that "delayed ejaculation is a common side effect of many psychotropic or antidepressant drugs." (McMahon et al., p. 1825, col. 1, ll. 13-14) The Answer selectively limits McMahon et al. and Lane to SSRIs, even though the actual disclosure of these references is a much broader class of drugs including serotonergic drugs, psychotropic drugs and

[3] Appellant's Contention 2 states "The rejection under 35 U.S.C. § 103(a) McMahon, Lane, Lilly and Robertson is based on an impermissible 'obvious to try' standard."

antidepressant drugs. The Answer goes on to state that "Eli Lilly and Robertson disclose finite embodiments of SSRIs as known in the art." This analysis is faulty, however, because the issue is not whether the Examiner can identify a secondary reference with a "finite number" since with the benefit of hindsight, the Examiner can identify a secondary reference that discloses a single embodiment. Rather, the issue is whether the skilled person has a finite number (as that term can be interpreted in view of the KSR facts) of options from which to choose. In this case, the disclosure of serotonergic drugs, psychotropic drugs and antidepressant drugs in McMahon et al. and Lane do not constitute a "finite number."

Further, by asserting that the "obvious to try" analysis from the KSR decision applies to the case, the Answer is also supposing that it is "predictable" how alternative solutions will work. The Answer asserts that McMahon et al. discloses treatment of premature ejaculation with paroxetine "on an as needed basis without a priming dose 3-4 hours prior to planned intercourse." (Answer, pp. 3-4, bridging paragraph) ***This assertion is not true.*** Nowhere in McMahon et al. is the term "priming dose" used. Moreover, the "as-needed" use of paroxetine in McMahon et al. was not structured to avoid a priming dose effect, and therefore, the study does not provide sufficient information for the skilled person to conclude that paroxetine is effective to treat premature ejaculation as-needed in the absence of priming doses. (Rivas Decl., ¶ 4.f.) The response to this point in the Answer is to argue that since McMahon et al. does not state that there is a need for a priming dose, one can conclude that there is not a need for a priming dose. (Answer, p. 6, ll. 1-4) This argument is not logical since the absence of a comment by McMahon et al. about priming doses only means that it was not addressed by McMahon et al., ***not*** that one can draw any conclusion about the need for priming doses.

Contrary to the Answer's position, McMahon et al. does not disclose treatment of premature ejaculation on an as needed basis that is effective without a priming dose. In fact, none of the cited references do. This position is strongly supported by the lead author of McMahon et al. who stated in 2005 that "[e]ffective, on-demand therapy that is effective within the time frame most suitable for the PE patient . . . is not currently available." (McMahon, C., J. Sex Med., Supp2:94-5 (2005)). Since there is no method known in the art for accomplishing the claimed invention, one

cannot conclude that it would be predictable that the invention would work as claimed. This is particularly true in an area of technology that is inherently unpredictable, such as pharmaceutical sciences. *See*, Gen-Probe Inc. v. Vysis, Inc., 2002 U.S. Dist. LEXIS 25020 at 67; *see also*, Pfizer, Inc. v. Apotex, Inc., 488 F.3d 1377 at 1384.

The Answer's reliance on the KSR decision and in particular, the "obvious to try" analysis is misplaced. The number of possible solutions (i.e., drugs affecting sexual function) for a skilled person to evaluate is quite large. There are no other known drugs that function as claimed (effective to treat PE on an as needed basis in the absence of priming doses) and there is no way for the skilled person to predict whether any given drug would successfully function as claimed. Therefore, it cannot be concluded that the use of dapoxetine would predictably solve the problem to be addressed.

Contention 3

The Answer does not address Contention 3[4]. Accordingly, Appellant's arguments that the time ranges for administration in claims 41, 42 and 52-54 are not merely optimization or discovery of workable ranges should be accepted, and the claims should be allowed.

Respectfully submitted,

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[4] Appellant's Contention 3 states "Administration of dapoxetine immediately prior to, to about 3 hours prior to a sexual activity is not mere optimization because efficacy of that dosing regimen is unexpected and the prior art teaches away from it."